Australian Government
Department of Health
Therapeutic Goods Administration

Consultation: Orphan drug program

2015 consultation outcomes and 2016 orphan drug program proposal

Version 1.0, October 2016

TGA Health Safety Regulation

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Contents

Purpose of September 2016 public consultation

The purpose of this consultation is to:

- present the outcomes of the initial orphan drug consultation conducted in 2015
- discuss proposed changes to the Australian orphan drug program
- seek feedback regarding specific aspects of the proposed program, which will be used to inform changes to the Therapeutic Goods Regulations 1990 which are required to implement the changes to the Australian orphan drug program

Stakeholders are invited to comment on six consultation questions.

Please specify:

- whether or not you support the proposed changes to the TGA orphan program. If you do not support the change/s, you may make suggestions for an alternative.
- an assessment of how the proposed change will impact on you, and what you see as the likely benefits or costs to you (financial or non-financial).
- if possible, please attempt to quantify these costs and benefits.

Consultation item 1 – rare disease threshold, seriousness of the condition:

A rare disease threshold of 5/10,000 (approximately 12,000 Australians) is proposed as one of two acceptable conditions for orphan designation. This is numerically less restrictive than currently (2000 Australians) and in isolation would allow more diseases to qualify as rare. In addition, the seriousness of the condition will be introduced as a new criterion for orphan designation, such that only conditions that are life threatening or chronically debilitating will qualify. The second and current option for sponsors to seek orphan designation based on a lack of financial viability independent of the rare disease threshold is proposed to be retained for conditions that are life threatening, seriously debilitating or serious and chronic. (Question 1, page 14)

Consultation item 2 – existing treatment and significant benefit over existing treatment:

The proposed orphan program introduces new criteria that aim to bring orphan products to market that treat conditions for which there is no existing treatment, or that can provide significant benefit over existing treatments. In this context, existing treatments would be established based on the Australian standard of care. If there are existing methods of treatment, the application must be supported by a justification of significant benefit over such treatments. Significant benefit can be demonstrated based on an assumption of improved efficacy, improved safety or a major contribution to patient care. (Question 2, page 14)

Consultation item 3 – orphan condition, medical plausibility and biomarkers:

Where the proposed orphan medicine is intended for only a subset of persons with a disease or condition, the TGA currently requests a justification of the medical plausibility as to why the remaining persons with the same disease or condition are not appropriate candidates for use of the medicine[i]. The concept of medical plausibility is proposed to be retained. The distinct condition is proposed, in alignment with EMA criteria, to be defined in terms of the specific characteristics, e.g. pathophysiological, histopathological, clinical

[i] <https://www.tga.gov.au/form/orphan-drug-designation-application-form>

characteristics. The genetic subtype/profile could additionally be included to define a subgroup. In general, subgroups would only be considered appropriate where the product would be ineffective or unsafe in the remaining population not having these characteristics. This applies equally where a biomarker is used to determine the subgroup. Defining a subset by reference to the fact that the drug will (or has) only been tested in a subgroup of patients would not be considered a sufficient justification for the restriction to a patient subgroup. (Question 3, page14)

Consultation item 4 – Paediatric populations:

Paediatric indications will continue to be considered for orphan designation, where the prevalence criterion is met in relation to the whole of the disease, or where the disease is different in the paediatric subgroup, or specific to the paediatric subgroup. Subgrouping based on the age of the sub-population would only be considered appropriate where the product would be ineffective or unsafe in the remaining population. The change in the rare disease threshold is expected to increase the number of paediatric conditions that may receive orphan designation. Paediatric indications that are not eligible based on the rare disease prevalence may be eligible for orphan status based on a lack of financial viability (criterion 1). (Question 4, page 14)

Consultation item 5 – Modifications to the designation process:

The key change to the designation process aims to align the timing of the assessment of eligibility for orphan designation closer with the date that the related registration application is lodged. The orphan designation is proposed to lapse within a set period, between 3 and 6 months of designation, if no registration application is lodged. This will ensure that the designation of orphan status is based on information that is current. Moreover, the designation can be withdrawn by the sponsor at any time. The TGA retains the right to cancel the designation at any time if there is evidence that the criteria for orphan designation are no longer met. (Question 5, page 16)

Consultation item 6 – Other considerations

Are there any other key issues that should be considered in developing the changes to the orphan drug program? (Question 6, page 16)

Background

The objective of the orphan drug program

When the orphan drug legislation was introduced in 1997 the intent was to provide an incentive to sponsors to bring medicines for a small population to market, and in doing so make medicines available to patients who would not otherwise be able to access such medicines. The incentive is in the form of waiving application and evaluation fees[ii].

In a broad sense the orphan drugs program can be considered a type of joint community service or public health obligation of the Government and prescriptions medicine industry. The original intention, as set out in the Explanatory Memorandum at the time of the amendment to the Therapeutic Goods Regulations in 1997, states that:

> *The Regulations... provide for an orphan drugs program by waiving fees in relation to the designation, evaluation and registration of orphan drugs, orphan drugs are drugs used in the treatment, prevention or diagnosis of rare diseases, and are often not commercially viable because of their small market potential. The amendments provide an opportunity for sponsors to market orphan drugs in Australia at a reduced cost through the waiving of application and evaluation fees...*

The program can be seen as part of a global movement to address treatment of approximately 7000 rare diseases worldwide (Seoane-Vazquez, 2008) with orphan drug programs launched in the US in 1983, in Japan 1993, and by the European Union in 2000 (Franco, 2013).

Box 1: The TGA orphan program

- 287 orphan designations were conferred in Australia (1998 to 2013)
- $35 million in fees were waived for registration applications for orphan drugs between 1998 and 2013
- The yearly average cost of the orphan drug program was estimated to be $3.9 million between 2011 and 2015 ($3.8 million for waived application and evaluation fees and $0.1 million for processing of designation applications)
- 86% of all orphan designation applications were approved and only 5% rejected. 66% of approved designations led to a registration application over a 5 year period (see Figure 1)
- Half of all approved designations (52%) were for haematological drugs and antineoplastic disorders (2011 – 2015)
- Types of orphan registration applications received: ~51% new chemical entities/new combinations, 41% extension of indication, 3% generics, 6% major variations
- The ratio of approved orphan to non-orphan submissions was 19:61

[ii] See regulation 45(12) of the Therapeutic Goods Regulations 1990.

(~1:3) in 2015 (based on extensions of indications and new entities)

- **The number of applications for orphan designation has increased by 78%** from an average of 14 designations per year (from program start to July 2008) to an average of 25 designations per year (2011 -2015), while total registration submissions have decreased by 14% over a comparable period (from 105 to 90 average submissions, based on new chemical entities or combinations and extension of indication). The data indicates a change in the relative proportion of orphans.

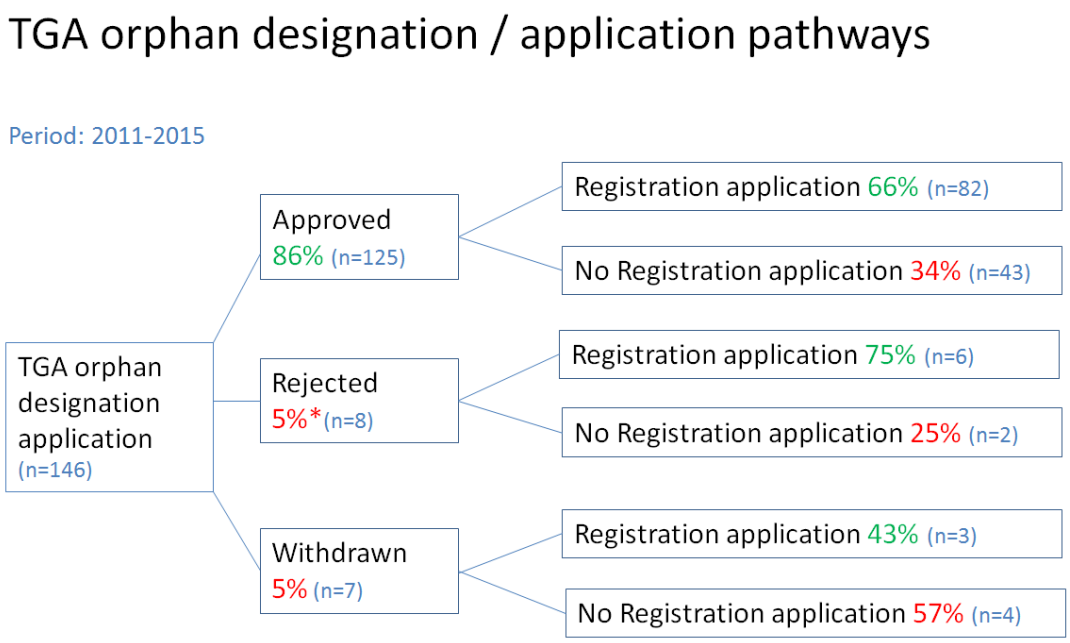
Developments in the orphan field

About 80% of all rare diseases have been estimated to be genetically based. A globally observed growth in orphan drug development has been linked to the improvements in technology to diagnose and identify rare diseases and subtypes of diseases, with the ability to tailor therapies for these diseases and disease subtypes. Consequently, a global increase in the number of applications for orphan drug designation and applications for market authorisation for such drugs has been observed (Boycott, 2013), (Reardon, 2014).

When the orphan drug program commenced in Australia it was more common to rely on broader indications and "whole" diseases. More recently, it is common for orphan indications to be very narrow either through being for a molecularly defined subset of a disease or limited to very specific stages of a disease. In Australia, the number of applications for designation has increased by 78% from an average of 14 designations per year to an average of 25 designations per year (2011-2015).

The increase in the number of orphan applications is predicted to continue. In addition, development of drugs for orphan conditions has been considered a viable business mode for some pharmaceutical companies (Meekings, 2012). Between 2015 and 2020 the market for orphan drugs is estimated to grow by 11.7% per year to $178 billion, based on an analysis of products expected to generate more than 25% of their sales from orphan indications. The same report predicts orphan drugs to account for 20% of global non-orphan prescription sales by 2020 (Reuters, 2012). It is therefore timely to consider changes to the TGA's now almost 20-year-old orphan drug program.

Figure 1: Orphan designation applications and related orphan registration applications received by TGA between January 2011 and December 2015 (<1-5 year follow up)



*14% of orphan designation applications, were not approved (8 rejected, 7 withdrawn, 6 progress)

Current Orphan legislation

The current definition of an orphan drug is set out in section 16H of the Therapeutic Goods Regulations 1990 (below) and has remained unchanged since the program commenced.

16H Orphan drug

1. A medicine, vaccine or in vivo diagnostic agent is an ***orphan drug*** if it complies with this regulation.

2. It:

   a. must be intended to treat, prevent or diagnose a rare disease;

   or

   b. must not be commercially viable to supply to treat, prevent or diagnose another disease or condition.

3. It is not an orphan drug if any of the following persons or bodies has refused to approve it for use for the disease for a reason related to the medicine's safety:

   a. the Secretary;

   b. the Food and Drug Administration of the United States of America;

   c. the Medicines Control Agency of the United Kingdom;

   d. the Bureau of Pharmaceutical Assessment of Canada;

   e. the Medical Products Agency of Sweden;

f. the Medicines Evaluation Board of the Netherlands;

g. the European Agency for the Evaluation of Medicinal Products.

4. It is not an orphan drug if it has been registered for use for the disease or condition before 1 January 1998.

5. However, it may be registered before 1 January 1998 for another use or indication.

A **rare disease** is defined in regulation 2 as a disease, or condition, likely to affect not more than 2,000 individuals in Australia at any time.

Regulation 16 I(4) concerning applications for designation as an orphan drug, requires: "for a vaccine or in vivo diagnostic agent, the application must also state that the vaccine or agent will be administered in Australia to not more than 2,000 people in each year after it is registered for use for the disease or condition."

Incentives

Regulation 45(12) provides a waiver of fees associated with an application for designation, for fees for the application for registration and for evaluation fees for the registration of a designated orphan drug.

Regulation 45

(12) The Secretary must waive the following fees:

a. a fee that would have been payable, but for this subregulation, for applying to the Secretary under subregulation 16I(1) to have a medicine designated as an orphan drug;

b. a fee that would have been payable, but for this subregulation, for the Secretary considering the application under regulation 16J;

c. a fee that would have been payable, but for this subregulation, as part of the registration of a designated orphan drug.

Outcomes of the 2015 public consultation

A paper on possible reform options for the orphan drug program was published for consultation in 2015. The options for reform included the patient threshold, the fee waiver and the criteria for orphan designation including subgrouping of indications. The purpose of the paper was to seek stakeholder input on whether the TGA orphan drug program is still fulfilling its intended purpose and, in particular, to seek feedback on four potential options for reform.

We received 21 responses in the consultation period from 1 May 2015 to 15 June 2015. Of those submissions, 9 were from pharmaceutical companies or regulatory affairs organisations, 9 from peak bodies (3 consumer / 2 industry /4 healthcare professional) and 2 from government bodies and one was an individual submission. All submissions that gave permission to be published are now available on the TGA website[iii]. The options presented were broadly:

[iii] <https://www.tga.gov.au/submissions-received-orphan-drugs-program>

Option one

- Definition –retain the status quo
- Threshold – increase the patient threshold
- Charging model – retain the fee waiver on initial designation, but fees apply on later changes (e.g. extension of indication)

Option two

- Definition – restriction of disease stages
- Threshold – increase the patient threshold
- Charging model – retain the fee waiver on initial designation, but fees apply on later changes (e.g. extension of indication)

Option three

- Definition – retain the status quo
- Threshold – increase the patient threshold
- Charging model – no fee waiver except in specific circumstances

Option four

- Definition – retain the status quo
- Threshold – increase the patient threshold
- Charging model – reduced fees (but not a full fee waiver) for designated orphan drugs.

Conclusions from the 2015 public consultation

There was no clear support for a particular one of the proposed reform packages. The majority of respondents supported a change to the orphan disease prevalence threshold that in isolation would allow more disease treatments to be classified as orphan. Restriction of the orphan designation to whole diseases was supported by few respondents, whereas several respondents were supportive of subgrouping orphan indications by disease subset and/or stage. Retaining the current 100% fee waiver for application and evaluation fees received more support than other charging model options. The overwhelming majority of respondents were in support of some form of fee waiver.

Because the TGA is fully cost-recovered from industry, any waiver of fees by TGA for orphan drugs in effect shifts the cost of the work done by TGA in orphan drug evaluation to sponsors of other products. For example, the waived TGA evaluation and registration fees for a new chemical entity and an extension of indications amount to $231,200 and $137,400 respectively[iv] at the current rate.

[iv] Current fees as of 1 July 2016

For the orphan program to remain financially viable, taking into consideration predicted increases in the number of applications with orphan status, the change to the orphan threshold supported by the majority of respondents would need to be balanced by the introduction of additional selection criteria that will serve to constrain the number of eligible applications.

Consultation proposal: adoption of EMA criteria with process modification

The objective of the proposal is to ensure that the overall orphan program objectives are continuing to be met and that the program remains viable as pharmaceutical drug development moves towards more targeted treatments. The EMA has recently assessed their orphan drug program to be successful in promoting access to orphan drugs (Morel, et al., 2016). Adoption of EMA orphan criteria provides a fair orphan drug program that does not impede the availability of drugs for rare diseases. The proposed program aims at bringing orphan products to market for conditions with no existing treatment, or which have significant benefit over existing products, as well as considering the seriousness of the condition and the medical plausibility of the indication or subgroup.

Proposed criteria

The proposed criteria for orphan designation are described in Figure 2. All four criteria must be satisfied in order for a medicine to be eligible for orphan designation and include:

- a change to the rare disease threshold (from currently 2000 Australians to 5/10,000 which equates to ~12,000 Australians)
- criteria that are in addition to the rare disease prevalence threshold (i.e. a 'seriousness of the condition' ,'existing methods' or 'significant benefit', as well as medical plausibility for subgroups and indications including disease delineation)

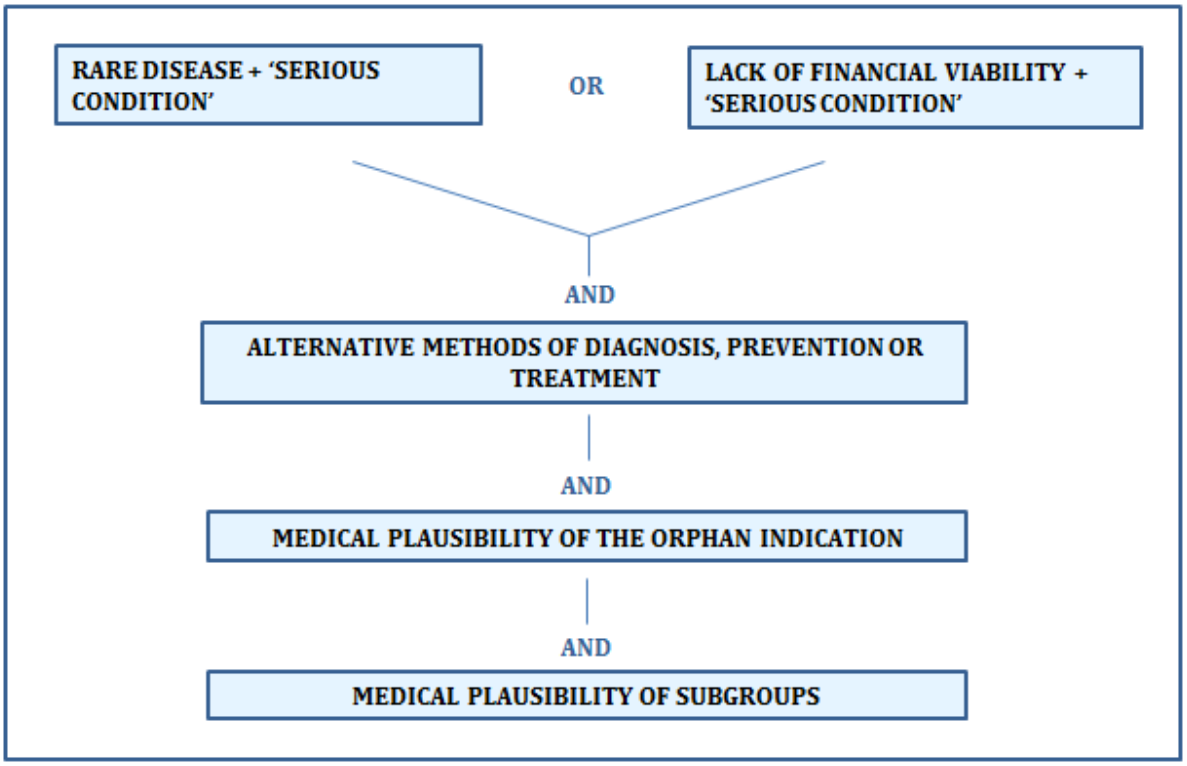
Table 1: Current and proposed rare disease thresholds

	'Rare disease' threshold	
	Individuals	**Ratio**
Current	2000	1/10,000*
Proposed (EMA criterion)	12,000**	5/10,000

*Intent of the program (1997)

**Based on an Australian population of just over 24 million (July 2016), more diseases could qualify

Figure 2: Proposed orphan designation criteria



Proposed incentive

1. 100% waiver of application and evaluation fees (*status quo*)

Proposed process

1. orphan designation lodged prior to registration (*current process*)
2. if the application for registration is not lodged within the set period (proposed to be between 3 – 6 months) after the designation, the designation lapses and the designation can be withdrawn or cancelled by the TGA if there is evidence that any criterion for orphan designation is no longer met (*new process*)
3. decision on designation application and any subsequent review to be made by the TGA's Principal Medical Adviser (*status quo*) who can seek external expert advice (including from the Advisory Committee for Medicines) in relation to the criteria (*new process*)
4. no fee for designation is planned (*current process*)
5. lodgement of registration application with orphan status can occur through any of the registration pathways that are either currently available, or the priority or provisional pathways that will be implemented based on the Government's response to the Expert Panel Review of Medicines and Medical Device Regulation.

Overview of the four proposed orphan designation criteria

Criterion one: Rare disease threshold or lack of financial viability and seriousness of the condition

EITHER

threshold of 5/10,000 (*less restrictive than status quo*, *more diseases may qualify as rare*) AND life threatening /chronically debilitating (*more restrictive than status quo*)

OR

life threatening /seriously debilitating or serious and chronic condition AND that without incentives it is unlikely that marketing would generate sufficient return to justify the necessary investment[v] (*more restrictive than status quo*)

The change in the rare disease threshold in isolation could allow more diseases to qualify as rare. In addition to meeting the prevalence criterion, the seriousness of the condition would be introduced as a new criterion for orphan designation, such that only conditions that are life threatening or chronically debilitating will qualify. The orphan program would continue to provide the option to apply for orphan designation where an orphan condition exceeds the patient threshold, based on lack of financial viability demonstrated as insufficient return on investment. The applicant would in addition have to demonstrate that the drug is for the treatment of a life threatening /seriously debilitating or serious and chronic condition.

Criterion two: Alternative methods of diagnosis prevention or treatment

There is no existing therapy (*more restrictive than status quo*)

OR

if there is existing therapy, the product represents a significant benefit over existing therapies[v] (*more restrictive than status quo*)

Orphan status is to be restricted to conditions with no satisfactory method of diagnosis prevention or treatment. Alternatively, significant benefit can be established if such methods exist. Significant benefit to those affected by the condition, i.e. a clinically relevant advantage through improved efficacy, or improved safety, or a major contribution to patient care is to be established based on comparison with the Australian standard of care (authorised treatments or established method). Significant benefit did not need to be demonstrated for 46% of EMA applications at the time of orphan designation decision (Morel, et al., 2016) indicating that at most about half of the designations may have been for novel treatments (i.e. there was no immediate comparator in the European context).

Criteria three and four: Medical plausibility

A justification for medical plausibility is required to support the orphan indication and to support subgrouping of indications.

[v] *Regulation EC No141/2000, EC No 847/2000*:

The orphan condition or disease needs to be based on aetiology, pathogenesis, pathophysiology, histopathology and clinical characteristics supported by international disease classification systems such as the WHO international classification of diseases code (ICD-10 code), where available.

In addition, any restriction of the proposed use of the orphan drug to a subset of a disease or condition would need to be supported by a justification of medical plausibility of why the use of the orphan drug would not be effective or safe when used in the rest of the population affected by the condition. The fact that the drug will (or has) only been tested in a subgroup of patients would not be considered a sufficient justification for the restriction to a patient subgroup.

Question 1: Do you support criterion one?

Question 2: Do you support criterion two?

Question 3: Do you support criteria three and four?

If you do not support the change/s, you may make suggestions for an alternative. Please provide an assessment of how the proposed change will impact on you, and what you see as the likely benefits or costs to you (financial or non-financial). If possible, please attempt to quantify these costs and benefits.

Paediatric indications will continue to be considered for orphan designation, where the prevalence criterion is met in relation to the whole of the disease, or where the disease is different in the paediatric subgroup, or specific to the paediatric subgroup. The change in the rare disease threshold in isolation could increase the number of paediatric conditions that classify as rare.

Question 4: Do you support the proposed consideration of paediatric indications?

If you do not support the change/s, you may make suggestions for an alternative. Please provide an assessment of how the proposed change will impact on you, and what you see as the likely benefits or costs to you (financial or non-financial). If possible, please attempt to quantify these costs and benefits.

Unchanged TGA incentives

The current incentive, in the form of a 100% application and evaluation fee waiver, has successfully served as the TGA incentive for sponsors to bring orphan drugs to market in Australia since the inception of the orphan program and is proposed to be retained.

Box 2: Proposed modifications to the EMA process reflecting adaptation to the Australian context

1. **Changes to the designation process:**
   - the orphan designation will lapse within a set period if no registration application is made
   - the designation can be withdrawn by the sponsor or cancelled by the TGA if any of the criteria are demonstrably no longer satisfied at any time
2. **No Changes to the TGA incentives:**
   - The current 100% waiver is proposed to be retained.

Modified designation process:

The EMA receives a higher number of orphan designation applications than the TGA on an annual basis. In 2015 approximately 10-times the number of designation applications was received by EMA (258)[vi] compared to TGA (25), The number of EMA market authorisations and TGA registrations with orphan status is more similar (9[vii] vs. 19; yearly average 2011-2014). Key reasons for the higher number of designations by the EMA could be due to the early stage at which designations may be sought (~25% of EMA orphan designations are based on preclinical data (Morel, et al., 2016)) and the large number of incentives including market exclusivity and protocol assistance. With the absence of incentives other than a fee waiver, it is unlikely that the TGA would receive similarly high numbers of designation applications.

Due to the differences in the funding models of the two regulators, process modification to adapt the EMA orphan program to the Australian system is required. In the Australian context it is proposed that the orphan designation will lapse if the application for registration is not lodged within a set period after designation (proposed to be between three to six months).

In 2011-2015 30% of orphan designation applications were lodged within 3 months of designation, 57% within a year, 9% within 1-5 years and 34% of sponsors had not lodged a registration application within a 5-year period. The requirement to lodge the designation application within a specified period of lodging the orphan registration applications, combined with automatic lapsing of the orphan designation after a set period (3 – 6 months) will mean that the supporting data remain current and should discourage premature applications.

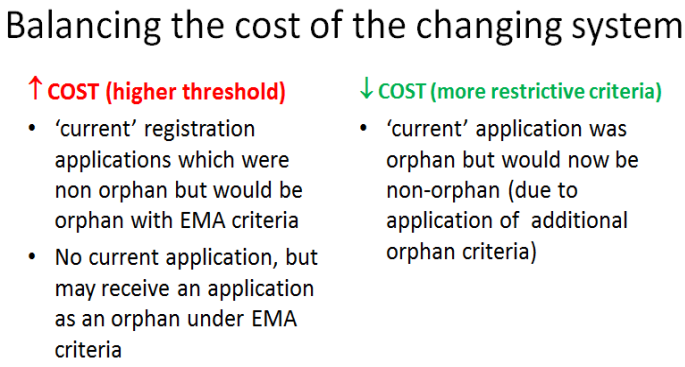
The designation can be withdrawn, or cancelled by the TGA, in the event that any of the criteria are demonstrably no longer valid. This might occur where a competitor drug (which may or may not also have an orphan designation) is registered in the period after designation but before the decision is made on registration).

[vi] <http://www.ema.europa.eu/docs/en_GB/document_library/Other/2015/04/WC500185766.pdf> sourced 21-7-2016

[vii] <http://ec.europa.eu/health/files/orphanmp/doc/orphan_inv_report_20160126.pdf> sourced 21-7-2015

Question 5: Do you support the proposed changes to the designation process and the timing of automatic lapsing? If you do not support the change/s, you may make suggestions for an alternative. Please provide an assessment of how the proposed change will impact on you, and what you see as the likely benefits or costs to you (financial or non-financial). If possible, please attempt to quantify these costs and benefits

Figure 3: The effect of increasing the population threshold is predicted to be minimal when counterbalanced by implementation of EMA's additional criteria that support bringing orphan products for conditions with no existing treatment, or significant benefit over existing products to market.



Predicted impact

Consequences of adopting EMA orphan criteria

Applications that, in comparison to Europe, are potentially excluded from reaching orphan status in Australia, due to the more restrictive rare disease threshold, would no longer be excluded. Adoption of EMA criteria would also exclude some medicines that would currently receive orphan status (**Figure 3**). The analysis (**box 3**) predicts no major impact on overall application numbers and program cost.

Question 6: Are there any other key issues that should be considered in developing the changes to the orphan drug program? If you do not support the change/s, you may make suggestions for an alternative. Please provide an assessment of how the proposed change will impact on you, and what you see as the likely benefits or costs to you (financial or non-financial). If possible, please attempt to quantify these costs and benefits

Box 3: Predicted effects of adopting EMA criteria on the TGA orphan program (2011-2014)[vii; viii]

Effect of 5/10,000 threshold on TGA orphan registration applications
Increase in threshold from 2000 Australians to currently ~12,000 Australians (5/10,000) is predicted to cause an increase in orphan registration applications

- 8 of 37 (21%) of all EMA market authorisations with orphan status granted between 2011 and 2014 did not have a TGA registration with orphan status or TGA orphan designation and an EMA orphan condition prevalence >0.83/10,000 (2000 Australians)
- Half (4) were registered on the ARTG following a non-orphan new chemical entity registration application (same or similar indication).
- The other half (4) were not registered in Australia; and under new criteria additional applications may be expected

Effect of additional EMA criteria on TGA orphan registration applications

- 23/78 (29%) of all approved TGA orphan registration applications lodged between 2011 and 2014 did not hold orphan status with the EMA, but had non-orphan market authorisation for the same active and the same or a similar indication.
- A yearly average of 2.5 new chemical entities and 3.25 extensions of indications would not have been lodged with orphan status if EMA criteria were applied
- Only 1 (4%) out of the 23 applications that this analysis was based on did not meet the life threatening or chronically debilitating criterion, suggesting that 'lack of existing treatment' or 'significant benefit if treatment exists' and medical plausibility of indication subsets are the key determinants of orphan status

Conclusion:

Overall, the retrospective analysis suggests that adoption of EMA orphan criteria would not have a major impact on the overall numbers of orphan registration applications. The increase in applications predicted due to a change in threshold would be balanced by a decrease in applications through a focus on bringing orphan products to market for conditions with no existing treatment, or that represent a significant benefit over existing treatment while ensuring medical plausibility for subsets.

[viii] To predict the impact of adopting EMA orphan criteria as part of the Australian orphan drug program, a retrospective 2-way gap analysis was conducted that compared prescription medicines with orphan designation approved by the TGA with those approved by the EMA, and vice versa, for the period of 2011-2014. The analysis is based on the assumption that the applications that held EMA market authorisation, but not EMA orphan status were not included in the EMA orphan program since they did not meet EMA orphan criteria. These products were marketed in Europe in the absence of orphan incentives.

Comparison of TGA and EMA orphan products

23 Australian orphan products were identified (2011-2014) that did not hold orphan status with the EMA, but had EMA market authorisation. Of these, 10 were new entities and 13 were extensions of indications. Approximately 70% of the drugs were for antineoplastic agents or antihaemorrhagics (**Figure 4**). Based on the new entity fraction of these (**Box 4**) the average PBAC sales (4/6) were $27,216,805 in the period of June 2015 to May 2016. In combination with the finding that 75% of the rejected TGA orphan designation applications (2011-2015) went on to lodge a non-orphan registration application for the same indication (**Figure 1**), it could be speculated that it is unlikely that the absence of TGA orphan status would have prevented product development for most of these products.

Box 4: Orphan sales for 2011-2014 antineoplastic new chemical entities with orphan status in Australia but not with the EMA[ix]

The new entity fraction of TGA orphan registrations between 2011 -2014 that held market authorisation but not orphan status with the EMA were analysed. 6 antineoplastic and 4 antihaemorrhagic agents were identified[x]. Australian sales estimates were calculated from the number of services for each PBS item number[xi], for the drug in question as recorded on Medicare Statistics, multiplied by the Dispensed Price for Maximum Quantity.

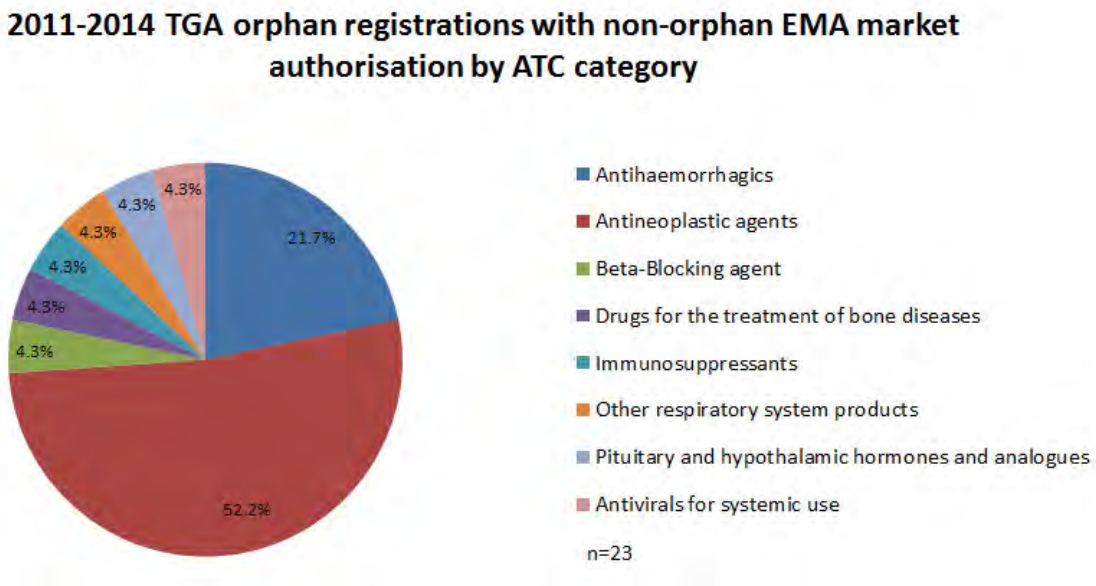
Active	PBS sales ($) May 2015 to June 2016
Drug 1	NO
Drug 2	5,420,754
Drug 3	22,336,444
Drug 4	NO
Drug 5	46,885,432
Drug 6	34,224,589

None of the 4 antihaemorrhagic dugs received PBS funding. None of the orphans that did not receive PBS funding were funded by the Life saving drugs program.

Conclusion: The Australian new entity orphan drugs that did not hold orphan status with EMA (presumably due to the selective action of the additional EMA orphan criteria) were associated with significant sales.

[ix] Items specific to the indication have been considered, however it is not possible to differentiate between indications for products with more than one entry on the general schedule since there is no certainty that the correct item number has been billed against, data should be taken as a general guide only.
[x] <http://medicarestatistics.humanservices.gov.au/statistics/pbs_item.jsp>
[xi] <http://www.pbs.gov.au/browse/medicine-listing>

Figure 4: The 2011-2014 gap analysis identified a number of TGA orphan drugs that had EMA non-orphan market authorisation represented by Anatomical Therapeutic Chemical Classification (ATC)



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Version history

Version	Description of change	Author	Effective date
V1.0	Original publication	Prescription Medicine Authorisation Branch	14 October 2016

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